UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,732	12/26/2006	Claudia Magagnoli	PP021455.0004 (2300-21455	5728

27476 7590 12/23/2009

NOVARTIS VACCINES AND DIAGNOSTICS INC.
INTELLECTUAL PROPERTY- X100B
P.O. BOX 8097
Emeryville, CA 94662-8097

EXAMINER	
GRASER, JENNIFER E	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
12/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,732	MAGAGNOLI ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,14-45,47 and 48* is/are pending in the application.

4a) Of the above claim(s) *15-42,47 and 48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12, 14 and 43-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Acknowledgment and entry of the Amendment submitted on 5/3/04 is made. Claims 1-12, 14, and 43-45 are currently under examination.

Claims 15-42, 47 and 48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claim Rejections - 35 USC § 112-Scope of Enablement

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-12, 14, and 43-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "a composition comprising an isolated LTK63 protein and arginine phosphate and CHAPS", does not reasonably provide enablement for compositions comprising *any* bARE protein with *any* stabilizing agent or wherein the stabilizing agent is *any* charged or uncharged amino acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification has demonstrated that the particular agents, arginine phosphated and CHAPS work to greatly stabilize the LTK63 protein. The specification has not demonstrated that said agents would be effective in stabilizing any other bARE

class protein. The instant specification fails to enable any other composition with an effective stabilizing agent. The prior art (see Wang, W. International J. Pharmaceutics, 199, 185: 129-188; e.g., 'Conclusions') teaches that the stabilization of polypeptides in pharmaceutical areas is unpredictable and that trials and errors play major roles in finding an effective combination. The art is highly unpredictable. The instant claims encompass the use of any bARE protein with any stabilizing agent, any charged amino acid or any uncharged amino acid. The specification does not encompass the scope of these claims. It is unclear what structure is encompassed by an 'analog' of any charged or uncharged amino acid. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention."

Given the lack of guidance contained in the specification, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Response to Applicant's arguments:

Applicants have argued the following:

The claims as pending are directed to stabilized integral AB5 CT and LT toxin proteins. As well known to the skilled artisan and described in the specification, CT and LT holotoxins were, at the time of filing, known to be similar in structure and function. *See, e.g.,* pages 13-14, noting the well-characterized nature of CT and LT endotoxins and that these two proteins are "structurally, functionally and immunologically" similar, including in that LT and CT are immunologically cross-reactivite. Thus, the skilled artisan would know that any LT or CT protein could be stabilized as described in the specification.

Likewise, the skilled artisan, armed with the teachings of the specification and in view of the state of art, would know that a variety of stabilizing agents other than those exemplified can be used. *See, e.g.,* pages 18-28, including Table 8 showing that various charged and uncharged amino acids were tested and stabilized the claimed bARE proteins. The specification and art teach in detail how to make and use (e.g., by testing) any stabilizing agent and, as such, it is simply a matter of routine experimentation for the skilled artisan to identify suitable stabilizing agents other than those exemplified.

These arguments have been fully and carefully considered but are not deemed persuasive. The specification appears to only recite up to Table 7(b) so it is unclear what Table 8 Applicants are referring to in their response. The use of any stabilizing agent in a highly unpredictable art would take undue experimentation, akin to invention. The sole example of LTK362, arginine phosphate and CHAPS does not enable the use of ***any*** stabilizing age**nt. It is noted that claim 1 does not even recite a single stabilizing agent.** The specification teaches that there was a long felt need in the art for a suitable means to stabilize the bARE class proteins. There is established unpredictability among agents. Accordingly, the broadly recited 'any stabilizing agent, including any charged or uncharged stabilizing agent or any charged or uncharged amino acid is not enabled. . Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing

out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention."

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 2, 6-8, 12-14 and 43-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Pizza et al (US-A-2002/0044939).

Pizza et al teach compositions comprising substantially integral bARE class proteins and a stabilizing agent which is a zwitterionic agent. The mutated bARE class protein (CT, LT, see paragraph [0030]) is highly stable, i.e., remains substantially integral. Uncharged agents are taught. Pizz et al teach the AB5- LTK63 and LTK 72 proteins. The proteins are analyzed under non-dissociating conditions which differentiate between integral and dissociated bARE class proteins. Immunogenic compositions and methods of treatment are also taught.

Repsonse to Applicant's arguments:

Applicants argue that Pizza et al relate to the stability of the A subunit of LT in isolation. This argument is not commensurate in scope with the claimed invention. **It is noted that claim 1 does not even recite a single stabilizing agent.** The composition

of claim 1 reads on native bARE class proteins such as that taught by Pizza et al which were able to be produced in low amounts from both native cells and transformed E.coli cells. Paragraph [0030] teaches a protein which is highly stable, i.e., remains substantially integral.

5. Claims 1, 2, 6-8, 12-14, and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Pronk et al (J.Biochem.Chem. 1985. 260(25): 13580-13584).

Pronk et al teach compositions comprising substantially integral bARE class proteins and a stabilizing agent which is a zwitterionic agent. Uncharged agents are taught. See the abstract which teaches crystals of LT (a bARE class protein), which crystal is a composition comprising (next to the stabilizing agents $CdCl_2$ and KF) said bARE class protein in a substantially integral form (see for example, Table II). The term "immunogenic compositions" is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. **It is noted that claim 1 does not even recite a single stabilizing agent.** The composition of claim 1 reads on native bARE class proteins such as that taught by Pronk et al which were able to be produced in low amounts from both native cells and transformed E.coli cells as recited in the 'Results and Discussions' section on page 13580. Column 2, page 13581, teaches LT at varying soluble levels. It is taught that LT was most soluble at high pH and became less soluble as pH levels decreased.

This soluble, integral LT reads on the soluble bARE class protein taught in claim 1 which does not require a stabilizing agent.

Response To Applicant's arguments:

Applicants have argued that Pronk et al solely to crystalline LT whereas the instant claims are daran to soluble holotoxin. The composition of claim 1 reads on native bARE class proteins such as that taught by Pronk et al which were able to be produced in low amounts from both native cells and transformed E.coli cells as recited in the 'Results and Discussions' section on page 13580. Column 2, page 13581, teaches LT at varying soluble levels. It is taught that LT was most soluble at high pH and became less soluble as pH levels decreased. This soluble, integral LT reads on the soluble bARE class protein taught in claim 1 which does not require a stabilizing agent.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers

should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 8:00 AM-6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

/Jennifer E. Graser/
Primary Examiner, Art Unit 1645

12/17/09